Figure 1. Mean differences in DAS28 between drinking groups. A between non-drinkers and drinkers. B between non-drinkers and high-risk drinkers. C between low-risk and high-risk drinkers.

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POS0463

BEST CARDIOVASCULAR RISK CALCULATOR TO PREDICT ABNORMALITIES IN LEFT VENTRICULAR GEOMETRY IN RHEUMATOID ARTHRITIS

S. Lugo-Perez¹, J. R. Azpiri-López¹, D. Á. Galarza-Delgado², I. J. Colunga-Pedraza², N. Guajardo-Jauregui², A. B. Rodríguez-Romero², A. Cárdenas², J. A. Davila-Jimenez², H. Azpiri-Díaz¹, O. A. Cepeda-Ayala¹, A. Garcia-Heredia¹.
¹Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Cardiology, Monterrey, Mexico; ²Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma de Nuevo León, Rheumatology, Monterrey, Mexico

Background: A relationship between rheumatoid arthritis (RA) and the presence of abnormalities in left ventricular (LV) geometry such as eccentric remodeling has recently been determined, even in the absence of cardiovascular risk factors and before clinical manifestations (1). The 2016 European League Against Rheumatism (EULAR) recommendations that cardiovascular (CV) risk prediction models should be adapted by a 1.5 multiplication factor in RA patients. Risk prediction algorithms based on the CV risk factors (CVRF) have been an important tool for adopting preventive measures and intensifying therapies based on the estimated risk but their application in predicting cardiac structural abnormalities has never been studied.

Objectives: The aim of the study is to determine the CV risk calculator that best predicts alterations in ventricular geometry in RA.

Methods: A cross-sectional, observational study of 108 RA patients between 40-75 years (ACR / EULAR 2010 classification criteria). The QRISK3, OMNI-BUS, Framingham Risk Score Lipids (FRSL), Framingham Risk Score BMI (FRS-BMI) and Reynolds Risk Score (RRS) calculators were compared. The diagnostic performance was determined by ROC curves, and the discriminative capacity by the Area Under the Curve (AUC) 95% CI. The echocardiogram was the diagnostic gold standard. A p value < 0.05 was considered statistically significant.

Results: The prevalence of abnormalities in ventricular geometry was 38.9%. QRISK3 reported AUC of 0.656, 95% CI (0.550-0.762, $p=0.006$), cut-off point ≥ 4.6 , sensitivity of 73.8% and specificity of 54.5%, and likelihood ratio of +1.62. FRS-BMI showed AUC of 0.653, 95% CI (0.543-0.762, $p=0.008$), cut-off point ≥ 11.02 , sensitivity and specificity of 61.9% and 57.6% respectively, and likelihood ratio of +1.46. OMNI-BUS showed AUC of 0.635, CI 95% (0.525-0.746, $p=0.018$), cut-off point ≥ 3.8 , sensitivity and specificity of 57.1% and 68.2%. While RRS had AUC 0.644, 95% CI (0.534-0.755, $p=0.012$), cut-off point of 2.25, sensitivity of 47.6% and specificity 78.8%, and likelihood ratio of +2.24 (Figure 1 and Table 1).

Table 1. Discriminatory capacity of the different cardiovascular risk calculators.

Calculators (cut-off point).	AUC	CI 95%		p	Sensitivity	Specificity
		Inferior	Superior			
QRISK (≥ 4.60)	0.646	0.537	0.754	0.012	73.8%	54.5%
SCORE	0.591	0.475	0.706	NS	-	-
OMNI-BUS (≥ 3.80)	0.621	0.509	0.734	0.038	57.1%	68.2%
FRSL	0.594	0.480	0.707	NS	-	-
FRS-BMI (≥ 11.02)	0.642	0.530	0.754	0.015	61.9%	57.6%
RRS (≥ 2.25)	0.627	0.514	0.741	0.029	47.6%	78.8%

Figure 1. ROC curves of the different cardiovascular risk calculators.

Conclusion: The QRISK3 calculator showed the highest discriminative ability and sensitivity to predict abnormalities in LV geometry. However, all calculators demonstrated the need for a lower cut-off point to predict alterations in ventricular geometry. Our findings require adequate reproducibility in other population groups to determine the applicability of CV risk algorithms as predictors of structural alteration of LV.

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POS0464

IS IT POSSIBLE TO IDENTIFY INDIVIDUALS AT IMMINENT-RISK OF SUB-CLINICAL JOINT INVOLVEMENT?

A. Di Matteo¹, K. Mankia¹, L. Duquenne¹, E. Cipolletta², J. Nam¹, L. Garcia-Montoya¹, R. Wakefield¹, M. Mahler³, P. Emery¹.
¹Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom.,
²National Institute for Health Research Leeds Biomedical Research Centre, Leeds, United Kingdom; ³Polytechnic University of Marche, Rheumatology Unit, "Carlo Urbani" Hospital, Jesi, Ancona, Italy, Department of Clinical and Molecular Sciences, Jesi, Italy; ⁴United States, Inova Diagnostics, INC, San Diego, California, USA, San Diego, United States of America

Background: In anti-CCP antibody (Ab) positive at-risk individuals with MSK symptoms but without clinical synovitis, the detection of ultrasound (US) sub-clinical inflammation is associated with an increased risk of progression to inflammatory arthritis (IA) ¹. Studies suggest that in these at-risk individuals, MSK symptoms develop before subclinical joint inflammation occurs on US. As such, anti-CCP Ab positive individuals with MSK symptoms in the absence of clinical or sub-clinical inflammation may be at the critical time-point for preventive treatments, before joint inflammation occurs and eventually becomes established (i.e., before the 'second-hit' in RA pathogenesis); however, identifying these individuals is challenging.

Objectives: To identify, in second generation anti-CCP Ab (CCP2+) at-risk individuals with MSK symptoms, but without clinical or sub-clinical synovitis, predictors of US sub-clinical synovitis.

Methods: In 186 CCP2+ at-risk individuals with normal baseline US scan (i.e., no synovitis or bone erosions), and a complete dataset, US data were analyzed at 6, 12 months, then annually until occurrence of IA. US synovitis was identified according to the EULAR/OMERACT definitions². Relevant demographic (age and gender), clinical [early morning stiffness (EMS), tenderness in the small joints of the hands] and serological [anti-CCP2 Ab level, third generation anti-CCP Ab

(CCP3) and rheumatoid factor (RF)] data were collected at baseline. Regression analyses, Kaplan-Meier analysis and Log-Rank test were performed.

Results: US synovitis was detected in ≥ 1 longitudinal US scan in 69/186 (37.1%) at-risk individuals (median time to first developing US synovitis: 53 weeks, IQR 27.0–105.8; median number of joints with US synovitis: 2.0, IQR 1.0–2.0). As shown in Table 1, only anti-CCP3 Ab were significantly associated with development of US sub-clinical synovitis in the multi-variable analysis while borderline results were observed with age.

Table 1. Regression analyses for the development of US synovitis.

	Univariable analysis		Multivariable analysis	
	OR (95% CI)	p-value	OR (95% CI)	p-value
Gender (male)	1.02 (0.52–2.02)	0.95	/	/
Age	1.03 (1.01–1.06)	<0.01	1.03 (1.00–1.06)	0.03
Tenderness in the hands	0.86 (0.46–1.61)	0.64	/	/
EMS	1.60 (0.87–2.95)	0.13	/	/
Anti-CCP2 Ab (high titre)	2.79 (1.37–5.67)	<0.01	1.20 (0.50–2.89)	0.69
Anti-CCP3+	4.44 (2.28–8.66)	<0.01	3.30 (1.39–7.89)	<0.01
RF+	2.96 (0.46–1.61)	0.01	1.45 (0.68–3.11)	0.33

CCP2+ individuals with positive anti-CCP3 Ab show a significantly reduced sub-clinical synovitis-free survival rate compared with individuals with negative anti-CCP3 Ab (Figure 1). At 1- and 2-year follow-up, respectively 23.3% and 38.3% of individuals with dual CCP2/CCP3 positivity developed sub-clinical synovitis on longitudinal scans, compared with 8.4% and 13.3% of CCP2+ individuals with negative anti-CCP3 Ab ($p=0.01$) (Figure 1a).

Figure 1. Kaplan-Meier analysis shows US sub-clinical synovitis free survival time in CCP2+ at-risk individuals.

Similar results were observed in the subgroup of high level CCP2+ individuals. At 1- and 2-year follow-up, respectively 24.5% and 39.4% of high level CCP2/anti-CCP3+, but only 6.1% and 15.2% of CCP2+ individuals with negative anti-CCP3 developed sub-clinical synovitis on longitudinal scans ($p<0.01$) (Figure 1b).

Conclusion: In anti-CCP2+ at-risk individuals with MSK symptoms, anti-CCP3 antibodies improve prediction of imminent development of subclinical joint inflammation. This may represent the critical time-point for interventions to prevent the onset of joint disease. This is also a unique population for investigating the drivers of joint involvement in the development of RA.

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POS0465

DIFFERENT CLINICAL RELEVANCE OF ANTI-CITRULLINATED PROTEINS ANTIBODIES IN RA PATIENTS

A. Avdeeva¹, M. Cherkasova², E. Nasonov², ¹V.A. Nasonova Research Institute of Rheumatology, Early Arthritis Laboratory, Moscow, Russian Federation; ²V.A. Nasonova Research Institute of Rheumatology, Laboratory of Immunology and Molecular Biology Rheumatic Diseases, Moscow, Russian Federation

Background: Anti-citrullinated proteins antibodies (ACPA) are a broad group of antibodies, including antibodies to citrullinated fibrinogen, antibodies to cyclic citrullinated peptide (anti-CCP), antibodies to modified citrullinated vimentin (anti-MCV), antibodies to citrullinated α -enolase.

Objectives: To find a potential relationship between ACPA and disease activity, bone destruction, and ACPAs responses to various therapeutic regimens.

Methods: The study included 232 patients (pts) with rheumatoid arthritis (RA); 90 pts (74 women, Me; IQR age 53.0 (38.0–58.5) years had early RA, with mean disease duration 5.0 (4.0–9.0) months, DAS 28 5.3 (4.4–6.1); 142 pts had advanced stage of the disease (123 women, median age 51.0 (43.0–60.0) years, disease duration 56.0 (24.0–96.0) months, DAS 28 6.2 (5.5–6.8)). Pts with early RA received methotrexate (MTX) subcutaneously at average 17.5 mg dose once weekly. Pts with advanced RA received the following anti-B-cell therapy: 34 pts - rituximab (RTX); 20 pts - RTX biosimilar; 43 pts - tocilizumab (TCZ) in combination with conventional DMARDs. Serum anti-CCP and anti-MCV concentrations were measured using ELISA.

Results: 77 (85.6%) pts with early RA were high positive for anti-CCP, and 29 (70.7%) pts - high positive for anti-MCV. A positive correlation was found between anti-MCV and DAS 28 ($r=0.4$, $p=0.04$). As for advanced RA, 78 (80.4%) pts were high positive for anti-CCP, and 70 (79.5%) - for anti-MCV. There was a positive correlation between anti-MCV concentration and SDAI ($r=0.4$, $p=0.02$), as well as CDAI ($r=0.4$, $p=0.02$). No significant correlations were found between the anti-CCP levels and activity indices, anti-CCP and acute-phase parameters in both early and advanced RA groups. Higher total Sharp scores (96.5 (65.0–122.0)) were found in pts high positive for anti-MCV ($n=79$), compared to low-positive/negative (57.0 (31.0–88.0)), respectively, ($n=27$, $p<0.05$). anti-MCV levels dropped significantly in pts on RTX and TCZ therapy at weeks 12 and 24 after initiation of treatment, while high anti-CCP concentration persisted throughout the treatment (Table 1)

Table 1.

Indicators	Anti-CCP, U/ml	Anti-MCV, U/ml
RTX group, n=34		
- baseline	100,0 (37,9–100,0)	559,4 (139,2–1000,0)
- 12 weeks	100,0 (26,1–100,0)	295,9 (74,0–962,7) ¹
- 24 weeks	100,0 (29,0–100,0)	194,7 (58,3–844,8) ¹
RTX biosimilar group, n=20		
- baseline	112,7 (18,3–264,8)	392,6 (75,7–1000,0)
- 12 weeks	71,7 (12,4–161,6)	210,5 (40,3–940,6) ¹
- 24 weeks	61,3 (13,12–129,4)	153,8 (43,1–702,8)
TCZ group, n=43		
- baseline	354,8 (67,9–500,0)	762,3 (106,9–2393,1)
- 8 weeks	500,0 (84,4–500,0) ¹	266,6 (85,8–927,0) ¹
- 24 weeks	355,8 (39,8–500,0)	135,7 (27,0–662,1) ¹

Note: ¹ $p<0,05$ vs baseline

Conclusion: anti-MCV levels correlated with inflammatory activity and development of bone destruction, and were decreasing in pts on treatment. Anti-CCP was less responsive, showed minor changes during treatment, therefore its' thorough monitoring was not feasible.

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